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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,686	03/09/2001	Gary Van Nest	377882000900	9981

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EXAMINER	
BROWN, TIMOTHY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,686	VAN NEST, GARY	
	Examiner	Art Unit	
	Tim Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received August 19, 2004. Claims 1-6 and 8-15 are under examination.

The rejection of claims 1-6 and 8-15 under 35 U.S.C. §112, second paragraph, and claims 5 and 15 under 35 U.S.C. §103(a), has been withdrawn.

The following rejections are maintained: claims 1-6 and 8-15 under 35 U.S.C. §112, first paragraph; claims 1-4, 6 and 8-10 under 35 U.S.C. 102(e); and claims 11-14 under 35 U.S.C. §103(a).

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 8-15 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Undue experimentation is defined by a number of factors, including: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence

of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

Here, Applicant's invention is drawn to a method and kit for suppressing a RSV infection in an individual comprising administering, to the respiratory tract of the individual, a composition comprising an ISS. The ISS is between 6 and about 200 nucleotides, and it is not administered in conjunction with RSV antigen or immunostimulatory cytokines. The composition is administered in an amount sufficient to suppress RSV infection.

Based on the breadth of Applicant's claims, the invention may comprise suppressing a RSV infection in a RSV-infected human, by administering any 5'-CG-3' ISS. However, Applicant's invention only enables a method of suppressing a RSV infection in a mouse, comprising administering to the respiratory tract of the mouse, a composition comprising an ISS polynucleotide having the sequence of SEQ ID NO:1, wherein the composition is free of RSV antigen and immunostimulatory cytokines.

Although the level of skill in the art is advanced, it has not witnessed suppressing RSV infection in a human using an ISS. Currently, the art recognizes only a few treatments for human RSV infection including Ribavirin and passive immunotherapy (Rev. Med. Virol. (2004), 14, pp. 149-168, 152, 155). It is also worth noting that most examples of ISS therapy demonstrate that efficacy requires the co-administration of an antigen (see e.g. Vaccine (2004) 3098-3104; and Journ. of Vir. (2004) Vol. 78, No. 18 pp. 9624-9632). Thus, using the outcome of using an ISS without RSV antigen or immunostimulatory cytokines to treat human RSV infection cannot be predicted. Based on this unpredictability, one skilled in the art would have to rely heavily on Applicant's specification in order to practice the claimed invention. However, Applicant's

specification does not provide sufficient guidance for one skill in the art to avoid significant experimentation.

First, Applicant's specification does not provide a working example where an ISS was used to suppress ISS to suppress RSV infection in a human or similar animal model. Although Applicant has shown SEQ ID NO:1 is effective in suppressing RSV infection in mice, he has not demonstrated its efficacy in a human. Thus, there is no disclosure of an effective dose or schedule of administration for the successful treatment of a human RSV infection using an ISS.

Second, teaching the suppression of RSV infection in mice does not teach one skilled in the art how to suppress RSV infection in humans. This results because important physiological and anatomical differences distinguish mice from humans. These differences are manifested when murine and human or primate models produce different results for the same assay. This is especially true for compositions that are directed toward stimulating the immune system; the differences between human and mouse antigen recognition makes murine models a less reliable predictor for a composition's effect in a human (Drug. Discov. And Devel. 2004; 7, 4, pp. 40-44). In the present case, the specification teaches administering an ISS to the respiratory tract of a mouse. This does not provide sufficient guidance to the treatment of a human given that the surface area of the human respiratory tract is much greater, and that the human polyclonal immune system is physiogically distinct from the monoclonal immune system of a mouse. This immunological distinction is important because the invention's mode of operation is to administer an ISS is to stimulate the immune system of a subject. Thus, teaching the treatment of a RSV infection in a mouse does not teach one skilled in the art how to treat RSV infection in a human.

Turning to the sequence of the ISS, the specification does not enable one skilled in the art to use any 5'-CG-3' ISS to suppress RSV infection in mice or humans. This results from the fact that the specific activity of an ISS is determined by its length, sequence and the number/position of its CpG motifs (Am. J. Respr. Cell Mol. Biol. (2003) 28 pp. 645-647). Thus, there is a high level of unpredictability in applying an ISS to a specific infection. However, the specification does not provide adequate direction for overcoming this lack of predictability since it fails to provide working examples for the range of ISS claimed. As a result, practicing the full scope of the invention would require the skilled artisan to screen a tremendous number of 5'-CG-3' ISS in order to identify those that are capable of suppressing RSV infection.

Based on the foregoing factors, the specification fails to enable one skilled in the art to make and use the claimed invention without undue experimentation.

Claims 1-7 and 8-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's claims are drawn to a method of suppressing RSV infection in an individual comprising administering to the individual an a composition comprising a 5'-CG-3' ISS, wherein the ISS is administered without an antigen or an immunostimulatory cytokines, and wherein the ISS is administered in an amount sufficient to suppress an RSV infection. As noted above, the invention as claimed reads on suppressing a RSV infection in a human using any 5'-CG-3' ISS. The specification, however, does not disclose how one skilled in the art may use any 5'-CG-3' ISS to suppress human RSV infection. Working examples of a method having the

scope of the claimed invention are also lacking. Therefore, the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that Applicant had possession of the invention at the time the application was filed.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 8-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite in the recitation of "wherein RSV antigen is not administered in conjunction with the administration of said composition . . . ." This language is indefinite because one skilled in the art would know whether administering the claimed ISS, and an adjuvant, through different compositions and at different times would constitute administering the ISS "in conjunction with" an antigen. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6 and 8-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Davis et al. (US 6,406,705). Regarding claims 1-4, 6, 8 and 9, Davis teaches a method for

suppressing respiratory syncytial virus infection in an individual comprising administering an ISS to the respiratory tract of said individual (col. 8, lines 56-62; col. 15, line 65; col. 16, line 67; col. 17, line 1; and col. 31, lines 49-60), wherein said ISS is greater than 6 and less that 200 nucleotides in length (col. 4, lines 18-19), wherein neither a viral antigen nor an immunostimulatory cytokine is coadministered with said ISS (col. 3, lines 4-6), and wherein said composition is administered in an amount sufficient to suppress an RSV infection (col. 9, lines 29-32). Davis further teaches performing its method by administering an ISS having the sequence 5'-CACGTTCC-3' (col. 30, line 30). Davis also teaches administering the ISS to the nasal passages and the lungs (col. 31, lines 58-60).

Regarding claim 10, the Examiner notes that the limitation "wherein the suppression comprises a reduction of RSV titer in a biological sample from said individual" is inherent to the teachings of Davis for the reasons stated in the previous Office action.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 11-14 are rejected under 35 U.S.C. §103(a) as being unpatentable over Davis. Davis teaches all the limitations discussed under 1-4, 6 and 8-10. Davis does not expressly teach assembling the ISS sequence into a kit wherein said kit lacks RSV antigen and an immunostimulatory cytokine. However, assembling reagents in preparation for an experiment is well within the knowledge generally available to one skilled in the art. Moreover, assembling reagents ensures that all the components necessary for an experiment are present. Accordingly,

it would have been obvious at the time of Applicant's invention to assemble Davis' ISS into a kit in order to facilitate the execution of its method. Note the disclosure of Davis would serve as instructions for administering the ISS sequence.

Response to Arguments

Applicant's arguments regarding the enablement rejection of claims 1-6 and 8-15 are moot in view of the new enablement rejection presented above.

Applicant argues the rejection of claims 1-4, 6 and 8-14 under 35 U.S.C. §102(e) is improper because Davis does not teach administering an ISS without an antigen. Applicant notes that Davis states "the Th1 response can be induced using CpG DNA alone, or CpG DNA in combination with a non-nucleic acid adjuvant at the same or different site or at the same or different times." Applicant further notes that an "adjuvant," by definition, is co-administered with an antigen. Thus, Applicant reasons Davis does not teach administering an ISS without an antigen.

Applicant's argument ignores the text in Davis which states "the Th1 response can be induced using CpG DNA *alone, or* in combination with a[n]. . . adjuvant . . . ." Thus, Davis teaches administering an ISS without antigen, or any other adjuvant. Furthermore, the ISS in Davis is not administered "in conjunction with" RSV antigen or immunostimulatory cytokines as claimed by Applicant. This is because Davis states that its ISS may be administered "at the same or different site or at the same or different times" as an antigen.

Applicant argues that Davis does not teach the elements of the invention as they are arranged in the claims. In particular, Applicant notes that the portion of Davis offered for

teaching administering an ISS composition "in an amount sufficient to suppress an RSV infection" relates to treating HBV and not HSV. The Examiner respectfully submits that Davis teaches this feature through inherency. This is because Davis teaches an ISS having the same scope as the ISS that Applicant claims is effective in suppressing RSV infection. Thus, the ability to suppress RSV is inherent to the composition taught by Davis.

Applicant argues that Davis cannot anticipate the invention because it does not teach the invention with specificity. Applicant points to the fact that Davis discloses that its ISS is effective for treating influenza viruses, while the invention has been noted by the Office as lacking such utility. Applicant reasons that the invention therefore possesses unexpected specificity that is not taught by Davis. The Examiner respectfully submits that Applicant's argument is moot because the claims do not require the invention to distinguish between RSV and influenza viruses. Moreover, the invention is simply directed to administering an ISS without any adjuvants or immunostimulatory cytokines. Davis teaches each of these steps as noted in this Office action. Therefore, Davis anticipates the claimed invention.

Applicant's arguments with respect to the rejection of claims 5 and 15 under 35 U.S.C. § 103(a) are persuasive. This rejection is therefore withdrawn. The following comments are therefore responsive to Applicant's comments regarding the obviousness rejection of claims 11-14.

Applicant argues that the rejection of the claims under 35 U.S.C. § 103(a) as obvious over any combination with Davis is improper because neither Davis, nor the references of record, teach administering and ISS without the administration of RSV antigen or immunostimulatory

cytokines. The Examiner respectfully maintains Davis teaches this feature as noted above. Thus, the rejection of claims under 35 U.S.C. § 103(a) as obvious over Davis is proper.

Applicant also argues that the Office action's conclusion of obviousness is based upon improper hindsight reasoning. However, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Here, the Office action modified Davis to arrange its assay reagents into a kit. The motivation for this combination was to assemble assay reagents so that they would be available when required. The Examiner submits that it was well within the knowledge generally available to one skilled in the art that items could be gathered and arranged together so as to facilitate a task. Thus, the Examiner's combination was properly motivated.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tim Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tim Brown
Examiner
Art Unit 1648

tb

James C. Housel 11/29/04